PREPARATION AND CHARACTERIZATION OF NATURAL HYDROXYAPATITE FROM TILAPIA BONE AND SCALE FOR BIOMEDICAL APPLICATIONS

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Dedicated to my parents, my wife, my sibling, my supervisor, my co-supervisor and friends, who gave me everlasting inspiration, never- ending encouragements and priceless support towards the success of this study.

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ABSTRACT

Hydroxyapatite, HA ($Ca_{10}(PO_4)_6(OH)_2$) is well known as a calcium phosphate mineral phase which is widely used as an implant material. HA derived from natural sources have received considerable interest from researchers due to the presence of trace elements (CO_3^{2-}, Na^+ and Mg^{2+}) beneficial for bone metabolism. Thus, in the present work, HA from Tilapia *(Oreochromis niloticus)* bones and scales were successfully extracted by calcination technique in neutral atmosphere. In order to produce HA with close composition to human bone, the calcination parameters such as temperatures, holding time and heating rate were manipulated. Results obtained indicated that treatment at 600 °C for 1 hour with 10 °C/min increments showed better characteristics for the desired HA as determined by Field Emission Scanning Electron Microscopy (FE-SEM), X-ray Diffraction (XRD) and Fourier Transform Infra-Red (FTIR) analyses. The extracted HA contained nano-sized grains (72 nm and 65 nm) with high specific surface areas of 88 m^2/g and 57 m^2/g for the bones and scales, respectively. The study found that the broad and low crystallinity XRD peaks obtained corresponded to both HA samples and were related to the presence of nano-sized crystals and trace elements in a lattice structure. The substitution of carbonate ions in the phosphate and hydroxyl sites indicated the presence of AB-type carbonate in bones and scales. The calcination temperature was identified to have influenced the thermal stability of both extracted HA, where decomposition of HA to secondary phases such as β-TCP and CaO had occurred at 1200 °C. The presence of Mg^{2+} in the HA composition had accelerated its decomposition at the earlier temperature of 1000 °C. Meanwhile, varying the calcination holding time and heating rate had enabled control of the amount of CO_3^{2-} occurrence in the HA composition in range between 1 and 9 wt%. The presence of this ion had increased the degradability of the HA. In addition, Na^+ and Mg^{2+} also had significant impact on the bioactivity of the extracted HA. Thus, HA from fish bones was identified to be more bioactive than the HA from fish scales due to the presence of extra amounts of Na^+ and Mg^{2+} in the HA composition.

ABSTRAK

Hidroksiapatit, HA ($Ca_{10}(PO_4)_6(OH)_2$) terkenal sebagai mineral kalsium fosforus dimana ia digunakan secara meluas sebagai bahan implan. HA yang diekstrak dari sumber asli telah menarik perhatian penyelidik disebabkan mengandungi unsur surih (CO_3^{2-}, Na^+ and Mg^{2+}) yang bermanfaat untuk metabolisme tulang. Dalam kajian ini, HA dari tulang dan sisik ikan Talapia *(Oreochromis niloticus)* telah berjaya diekstrak dengan teknik pembakaran dalam keadaan atmosfera neutral. Untuk menghasilkan komposisi HA hampir dengan tulang manusia, parameter pembakaran seperti suhu, tempoh dan kadar pembakaran dimanipulasikan. Pembakaran pada suhu 600 °C selama 1 jam dengan kadar 10 °C/min mempunyai ciri-ciri yang terbaik, ini dapat ditentukan melalui Mikroskop Elektron Pengimbas Pancaran Medan (FE-SEM), Pembelauan Sinar-X (XRD) dan Spektrometer Infra-Merah (FTIR). HA yang diekstrak mengandungi bijian saiz nano (72 nm and 65 nm) bersama luas permukaan spesifik yang tinggi iaitu 88 m^2/g and 57 m^2/g bagi sampel tulang dan sisik ikan. Kedua-dua sampel HA memaparkan puncak yang lebar dan hablur rendah pada corak pembelauan XRD, ini disebabkan oleh kehadiran kristal bersaiz nano dan unsur surih di dalam struktur kekisi HA. Penggantian ion karbonat di tempat fosforus dan hydroksil menunjukan kehadiran jenis-AB karbonat di dalam tulang dan sisik. Suhu pembakaran didapati mempengaruhi ketidakstabilan fasa HA dari kedua-dua sumber, dimana penguraian HA kepada fasa kedua seperti Beta trikalsium fosfat (β-TCP) dan kalsium oksida (CaO) berlaku pada suhu 1200 °C. Kehadiran ion magnesium di dalam komposisi HA telah mempercepatkan proses penguraiannya pada suhu 1000 °C. Pengawalan tempoh dan kadar pembakaran dapat mengawal kandungan ion karbonat (CO_3^{2-}) di dalam komposisi HA. Kehadiran ion ini telah meningkatkan kebolehupayaan degradasi HA. Natrium (Na^+) dan Magnesium (Mg^{2+}) juga mempunyai impak yang signifikan terhadap kebolehupayaan bioaktif HA yang diektrak. Dimana, HA dari tulang ikan dikenal pasti lebih bioaktif berbanding sisik disebabkan oleh kehadiran Na^+ and Mg^{2+} yang lebih banyak di dalam komposisinya.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS AND ABBREVIATIONS

%	-	Percentage
°	-	Degree
°C	-	Degree Celsius
°C/min	-	Degree Celsius per minute
µm	-	Micrometer
ACP	-	Amorphous calcium phosphate
AGS	-	Average grain size
APS	-	Average particle size
APW	-	Average pore width
ASTM	-	*American Society for Testing and Materials*
BET	-	Brunauer–emmett–teller
Ca/P	-	Calcium/phosphorus
$Ca_{10}(PO_4)_6(OH)_2$	-	Hydroxyapatite
CaO	-	Calcium oxide
CB	-	Calcined bone
CDHA	-	Calcium-deficient carbonated apatite
CHA	-	Calcium carbonated apatite
Cl	-	Chlorine
CO_3^{2-}	-	Carbonate
CPV	-	Cumulative pore volume
CS	-	Calcined scale
EDX	-	Energy-dispersive x-ray
FB	-	Fish bone
FF	-	Fish fin
FH	-	Fish head
FS	-	Fish scale
FTIR	-	Fourier transform infrared

h	-	Hour
H_2O	-	Water
HAFB	-	Hydroxyapatite for fish bone
HAFS	-	Hydroxyapatite for fish scale
HAp	-	Hydroxyapatite
HIP	-	Hot isostatic pressing
HP	-	Hot pressing
HR	-	Heating rate
HTF	-	High temperature laboratory furnace
ICP-MS	-	Inductively coupled plasma-mass-spectrometre
JCPDS	-	The Joint Committee on Powder Diffraction Standards
K	-	Kelvin
MBM	-	Mammalian meat and bone meal
Mg	-	Magnesium
min	-	Minute
MPa	-	Megapascal
MWS	-	Microwave sintering
Na	-	Sodium
nm	-	Nanometer
OA	-	Oxyapatite
OH^-	-	Hydroxyl
PO_4^{3-}	-	Phosphate
PV	-	Pore volume
PW	-	Pore width
rpm	-	Rotation per minute
SBF	-	Simulated body fluid
SEM	-	Scanning electron microscopy
SSA	-	Specific surface area
TGA	-	Thermogravimetric analysis
Ti	-	Titanium
TSS	-	Two-step sintering
TTCP	-	Tetracalcium phosphate

UTS	-	Ultimate tensile strength
wt.%	-	Weight percentage
XRD	-	X-ray diffraction
α-TCP	-	Alpha-tricalcium phosphate
β-TCP	-	Beta-tricalcium phosphate
θ	-	Theta

CHAPTER 1

INTRODUCTION

1.1 Background of study

Osteoporosis is a common occurrence in adults and is characterized by a decline of bone mass and a microarchitectural deterioration of bone tissue (Woolf & Pfleger, 2003). It is estimated that more than one third of adult women will sustain one or more osteoporotic fractures in their lifetime as they pass through menopause (Cummings & Melton, 2002). The incidence of bone fractures worldwide is constantly increasing and approximately 200 million people in the world are already affected by osteoporosis (Pisani *et al*., 2016).

Bone grafts have been promoted as surgical intervention for bone fractures as a healing solution. There are three main types of bone grafts available: autografts, allografts and xenografts (Habraken *et al*., 2016). The most common of these bone grafts is the autograft, which is the transplanting of bone tissue from one site to another in the same patient. However, due to the necessity of additional surgery and restricted supply of autologous bone and risk of possible infection of the autograft, (Akram *et al*., 2014; Rodrigues *et al*., 2003) xenografts or synthetic substitutes were introduced as alternatives.

A xenograft is a graft of tissue transplanted from animal bone to human bone. The advantages of this material (xenogenous bone) are that it is easy to obtain, available at lower cost and almost in unlimited supply (Kusrini & Sontang, 2012). Xenogenous bones can be obtained from various animal sources such as bovine, porcine, fish bones and fish scales (Boutinguiza *et al*., 2012; Haberko *et al*., 2006; Niakan *et al*., 2015; Pon-On *et al*., 2016).

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